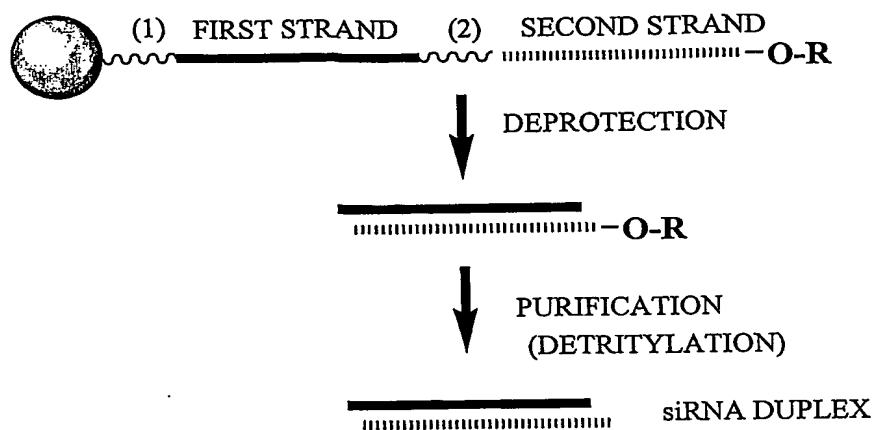


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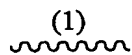
Figure 1

= SOLID SUPPORT

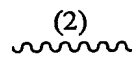
R = TERMINAL PROTECTING GROUP

FOR EXAMPLE:

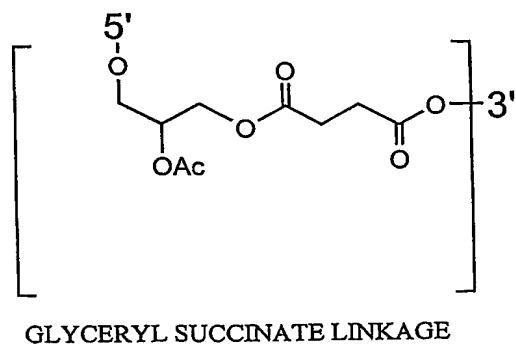
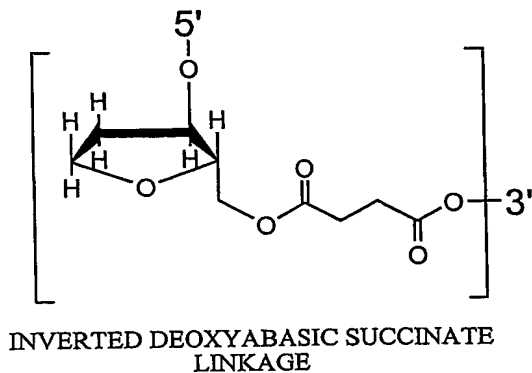
DIMETHOXYTRITYL (DMT)



(1) = CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

(2) = CLEAVABLE LINKER

(FOR EXAMPLE: NUCLEOTIDE SUCCINATE OR
INVERTED DEOXYABASIC SUCCINATE)

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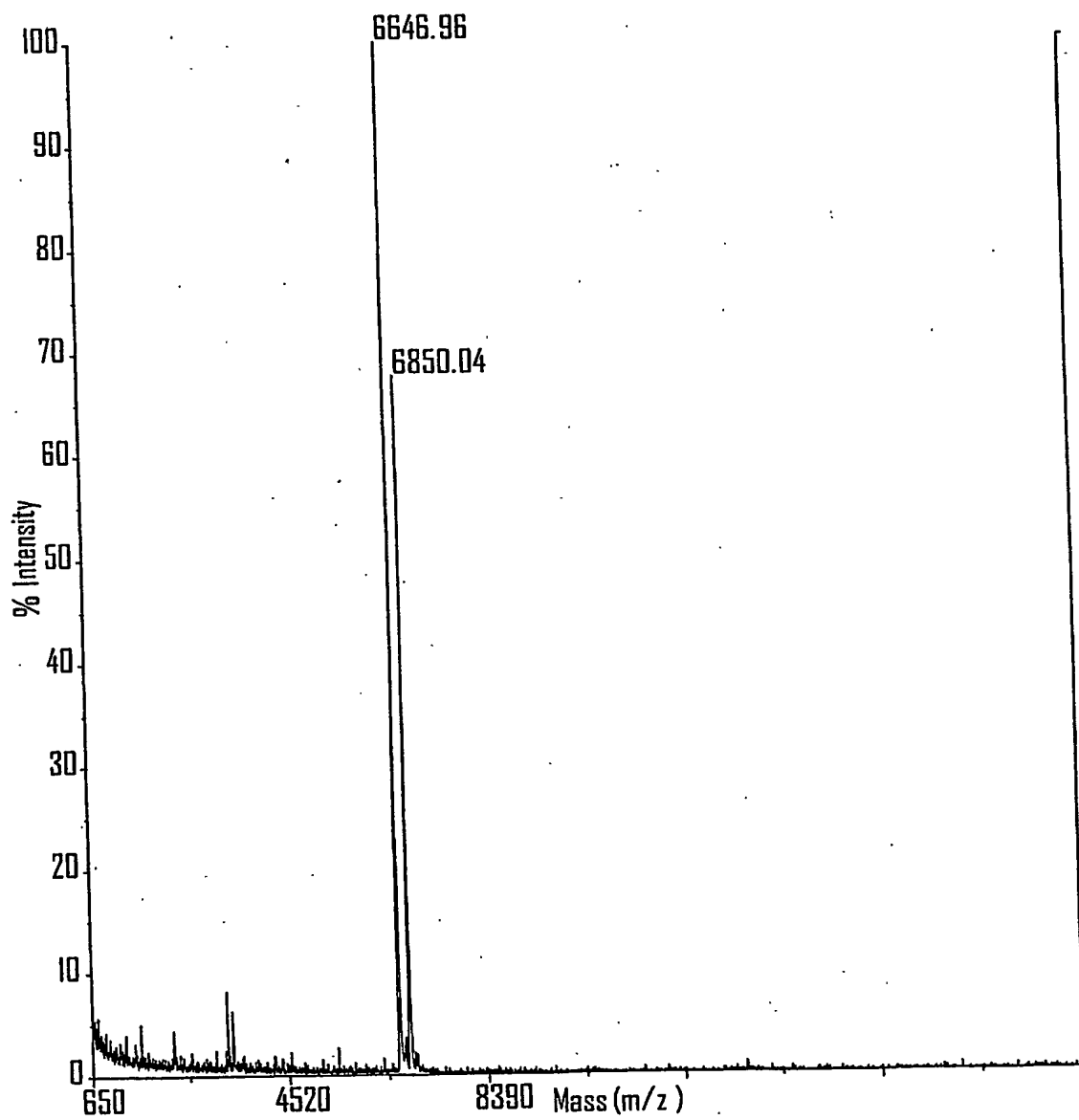
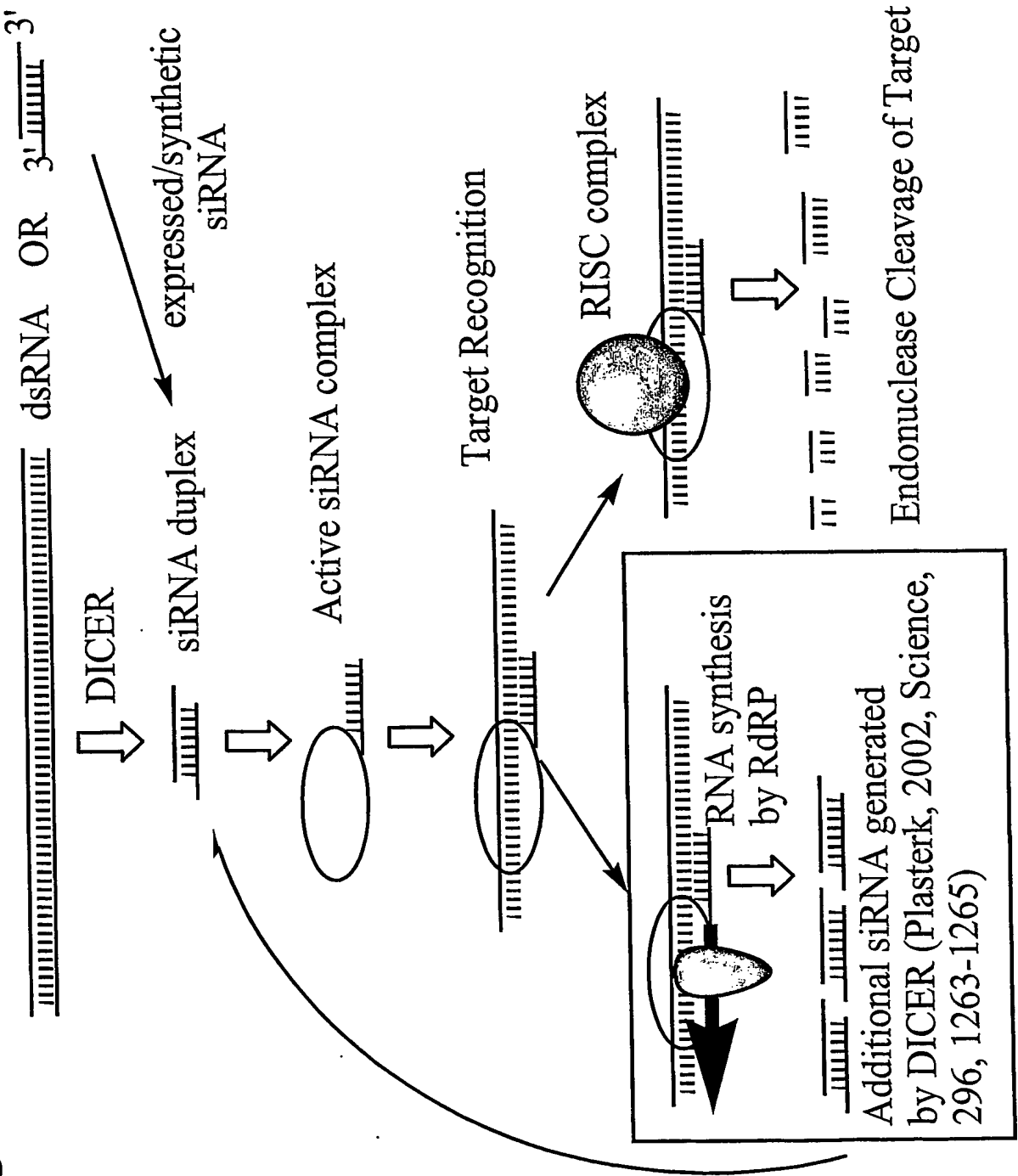
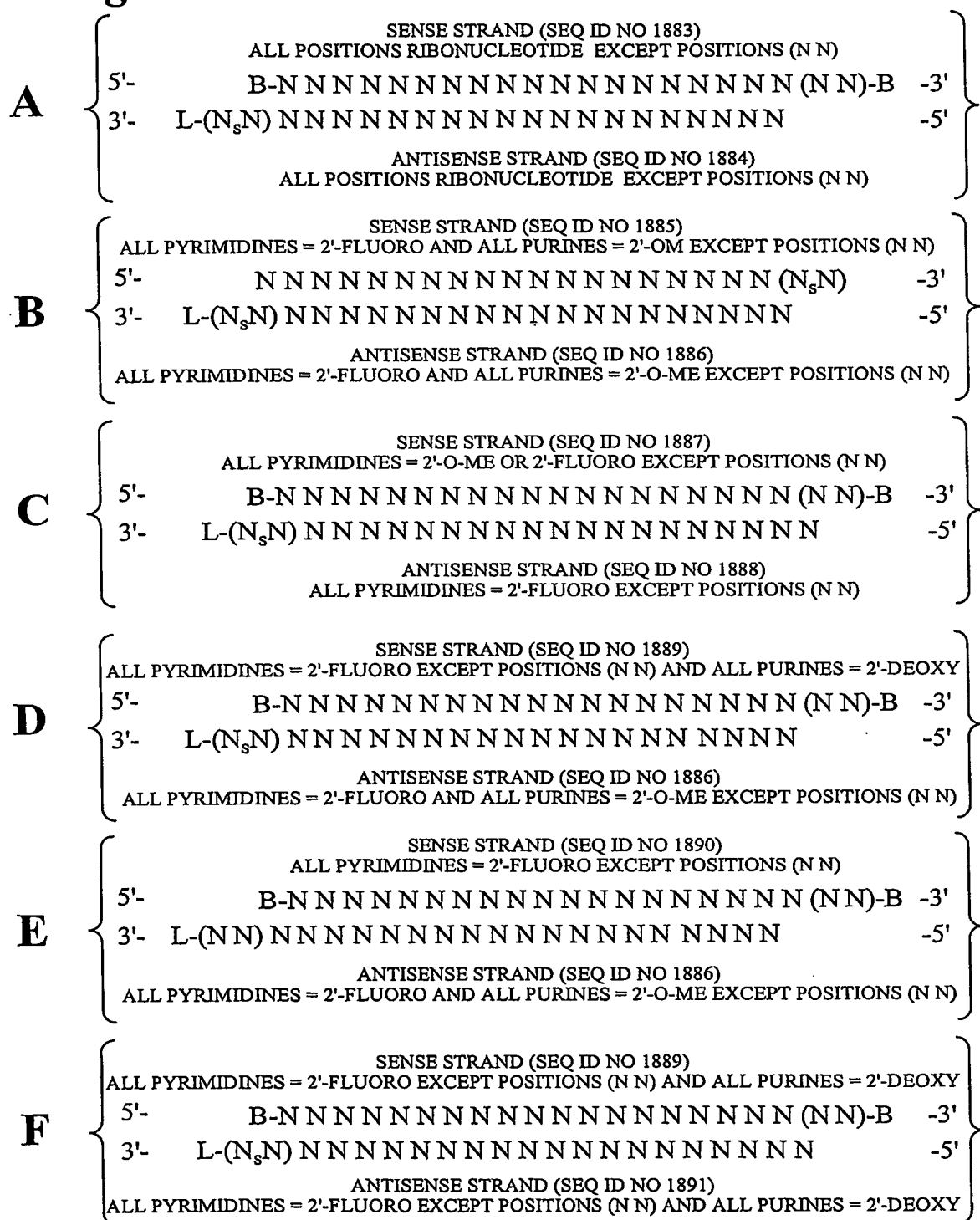
Figure 2

Figure 3



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Figure 4

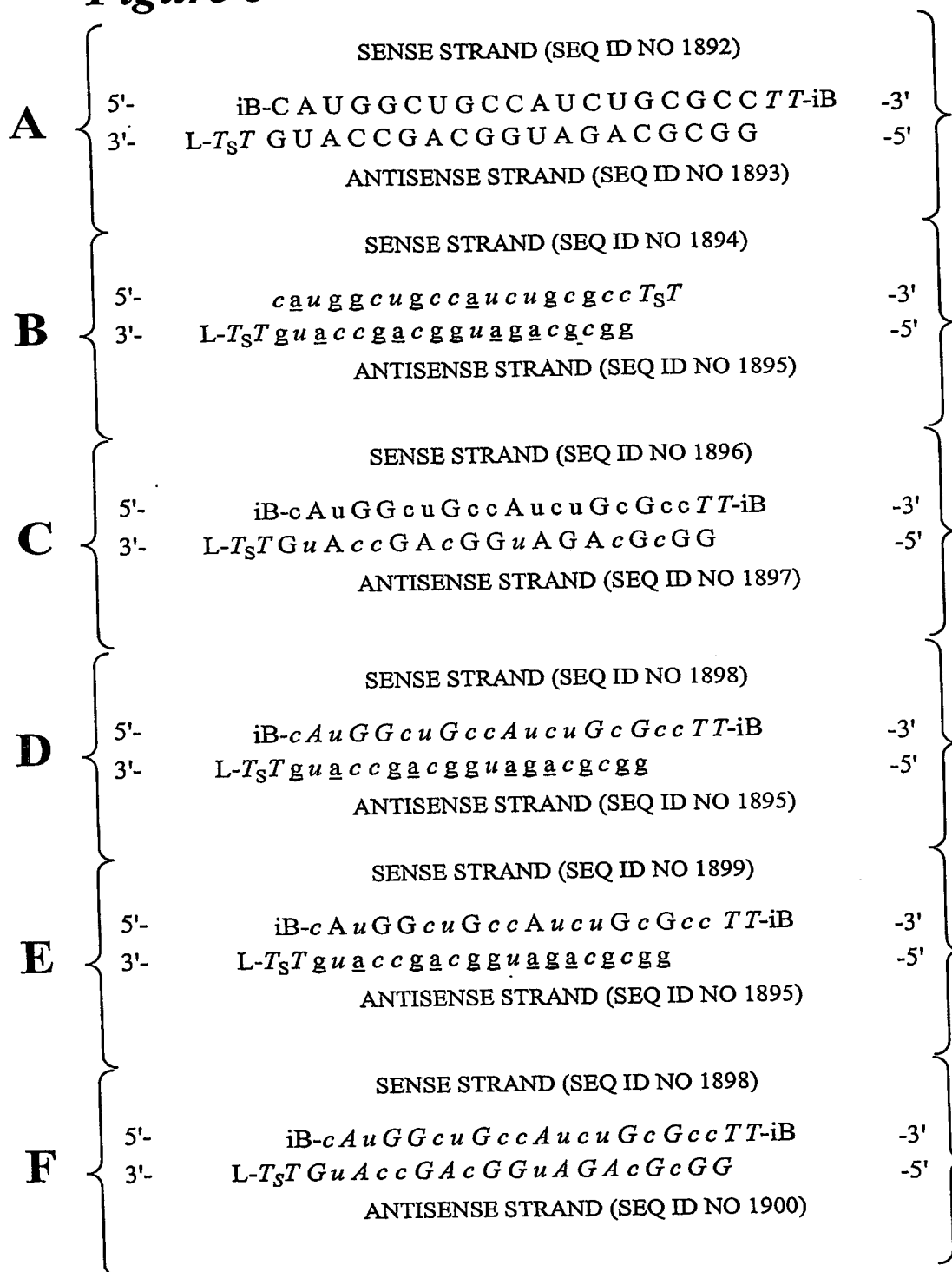
POSITIONS (NN) CAN COMPRISE ANY NUCLEOTIDE, SUCH AS DEOXYNUCLEOTIDES (eg. THYMIDINE) OR UNIVERSAL BASES

B = ABASIC, INVERTED ABASIC, INVERTED NUCLEOTIDE OR OTHER TERMINAL CAP THAT IS OPTIONALLY PRESENT

L = GLYCERYL OR B THAT IS OPTIONALLY PRESENT

S = PHOSPHOROTHIOATE OR PHOSPHORODITHIOATE THAT IS OPTIONALLY ABSENT

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Figure 5

lower case = 2'-O-Methyl or 2'-deoxy-2'-fluoro

italic lower case = 2'-deoxy-2'-fluorounderline = 2'-O-methyl

ITALIC UPPER CASE = DEOXY

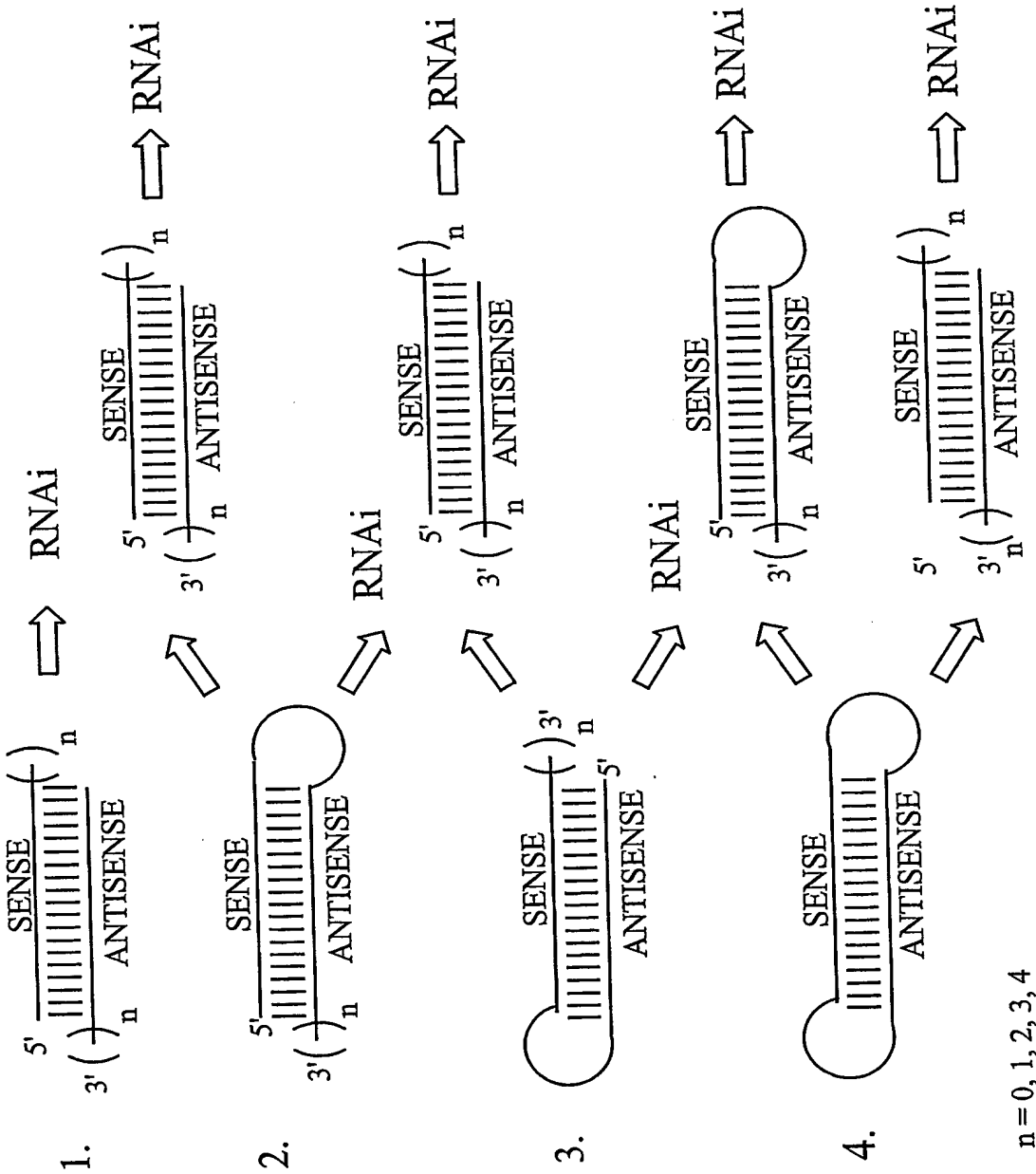
iB = INVERTED DEOXYABASIC

L = GLYCERYL MOIETY OR iB OPTIONALLY PRESENT

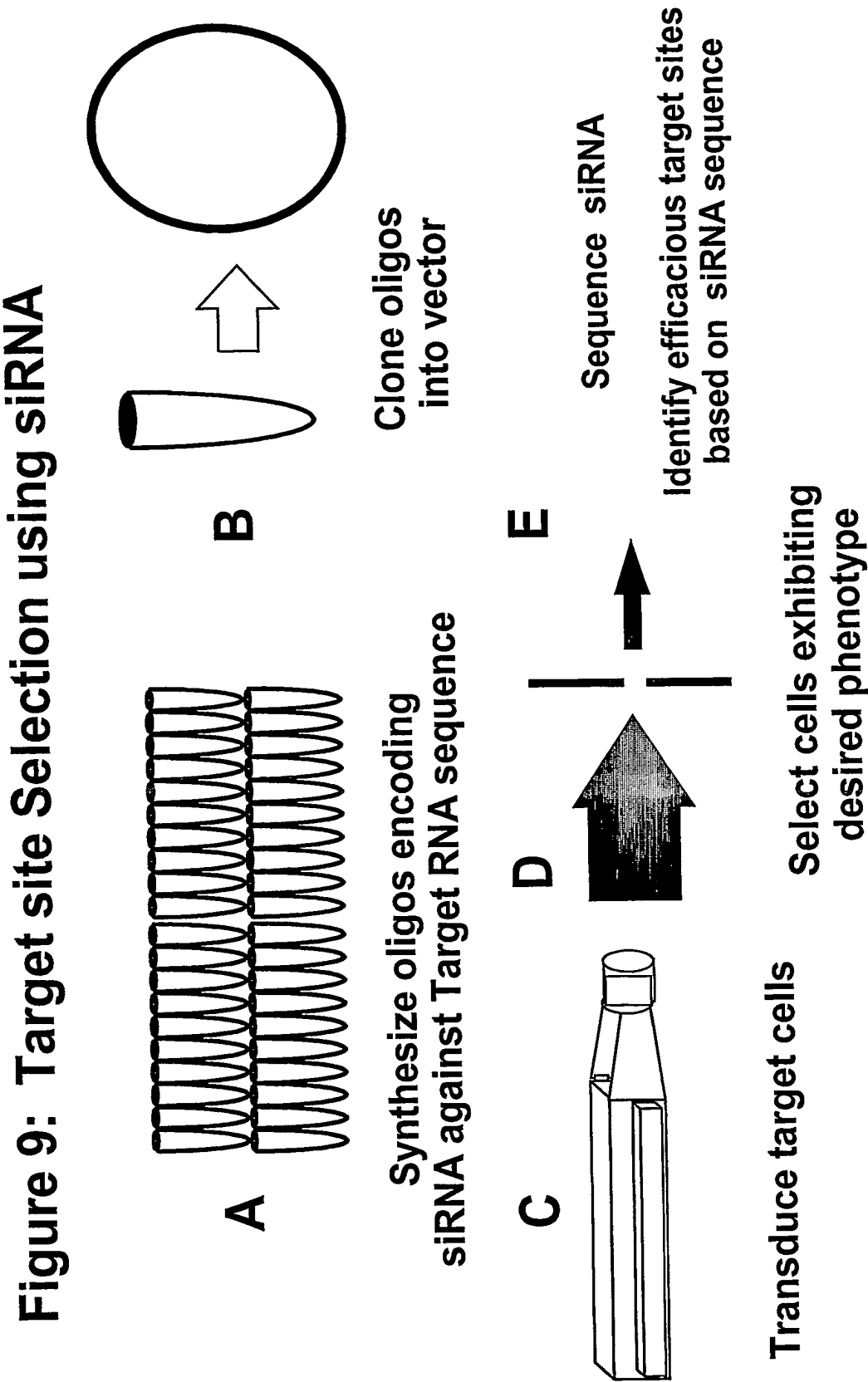
S = PHOSPHOROTHIOATE OR

PHOSPHORODITHIOATE OPTIONALLY PRESENT

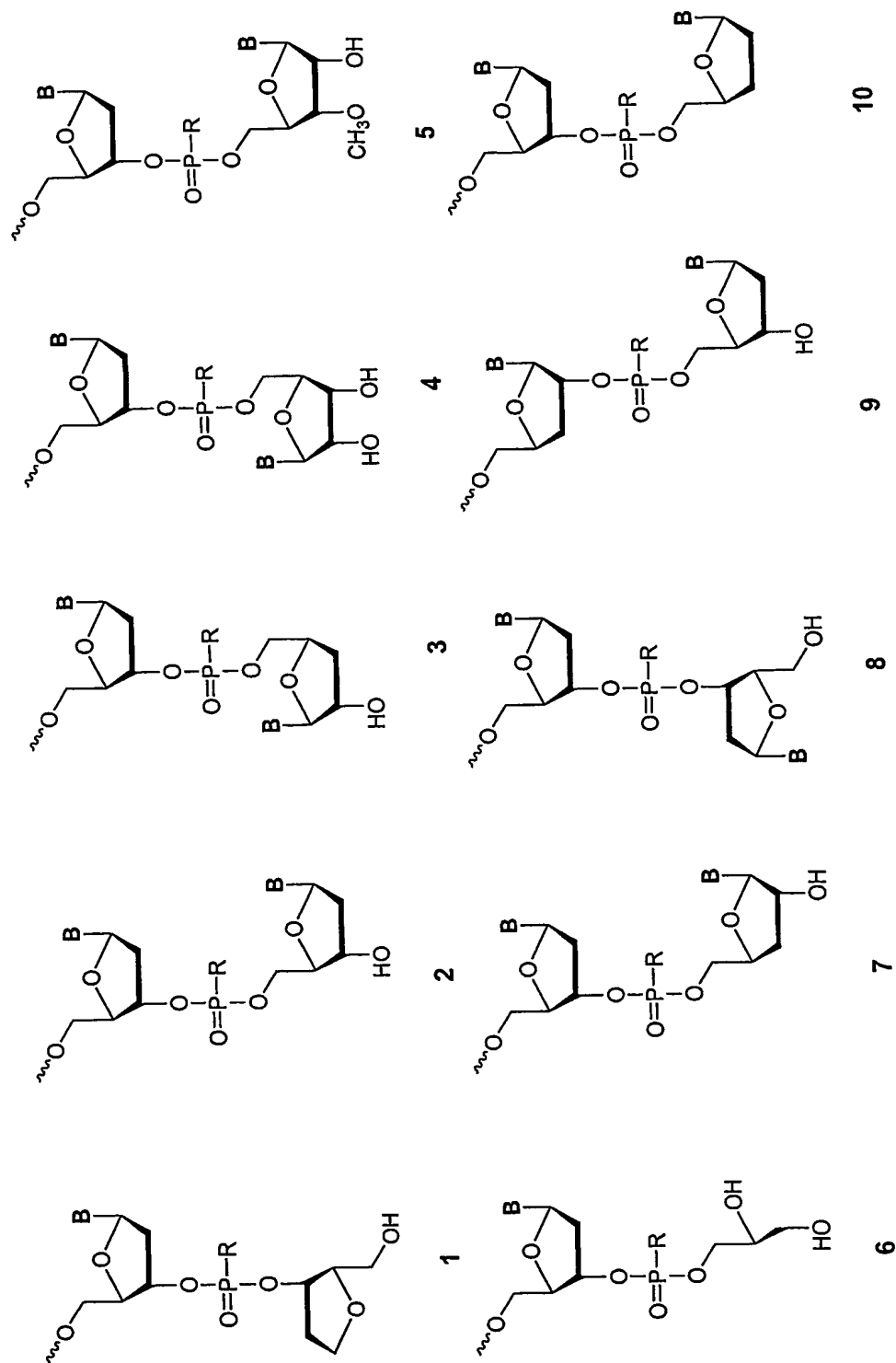
Figure 6



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Figure 10

R = O, S, N, alkyl, substituted alkyl, O-alkyl, S-alkyl, alkaryl, or aralkyl
 B = independently any nucleotide base, either naturally occurring or chemically modified, or optionally H (abasic).

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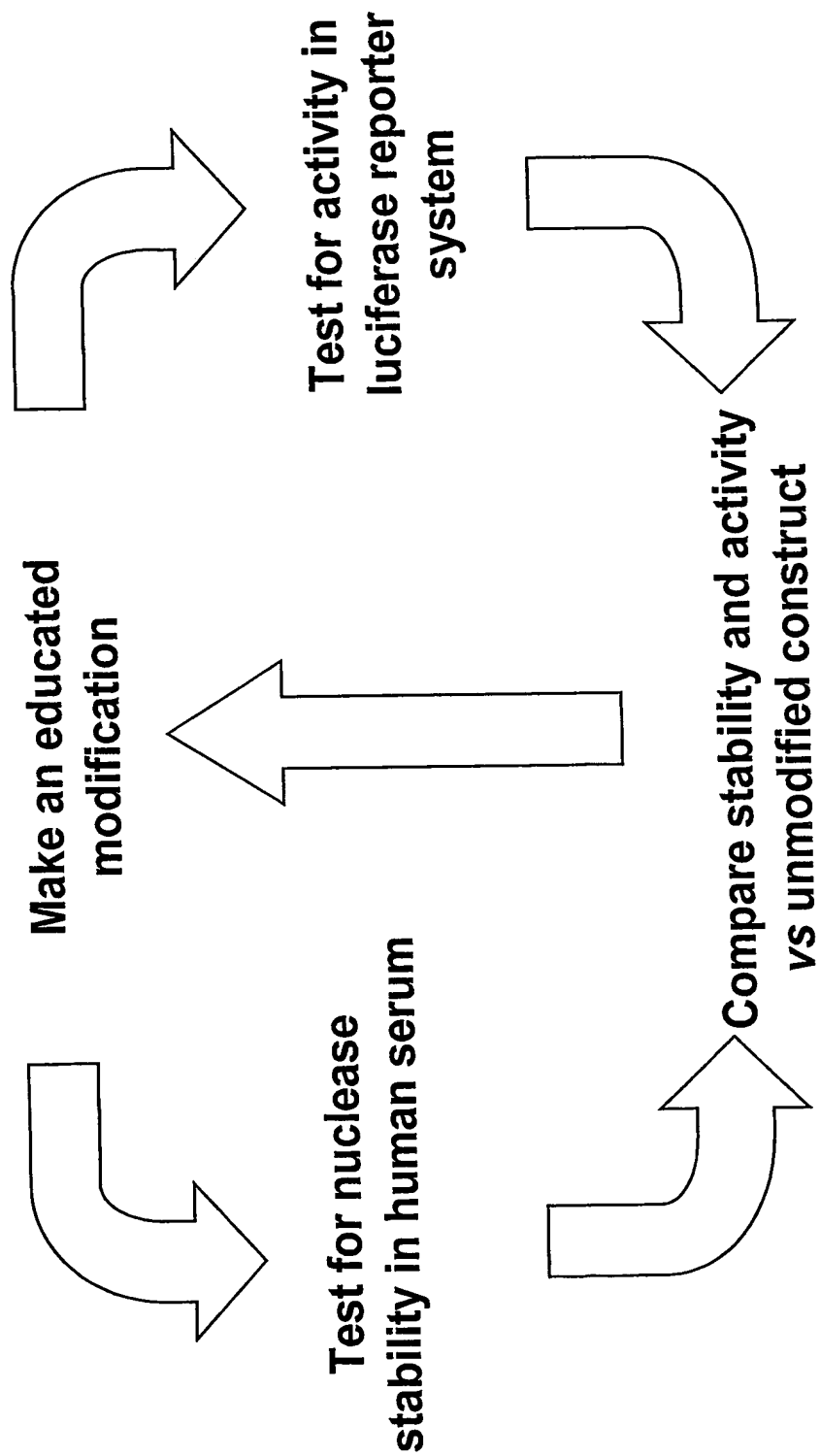
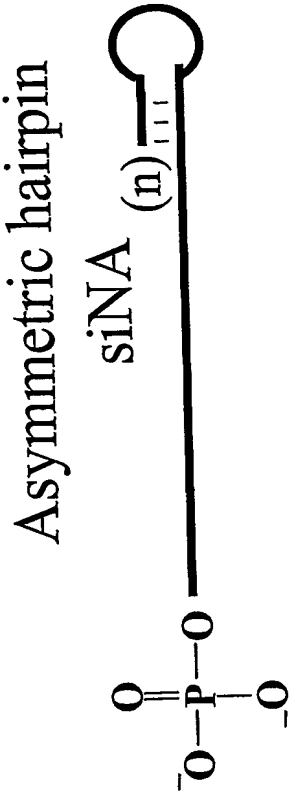
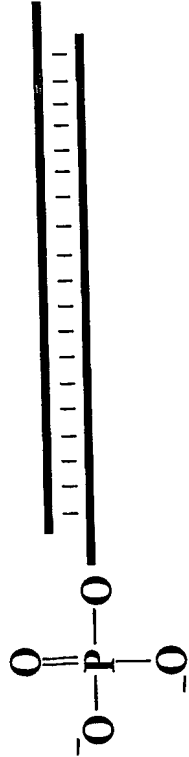
Figure 11: Modification Strategy

Figure 12: Phosphorylated siNA constructs



Phosphates can be modified
as described herein



Asymmetric duplex
siNA

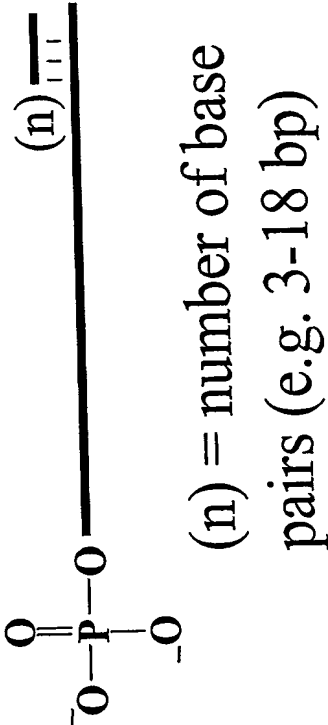


Figure 13: 5'-phosphate modifications

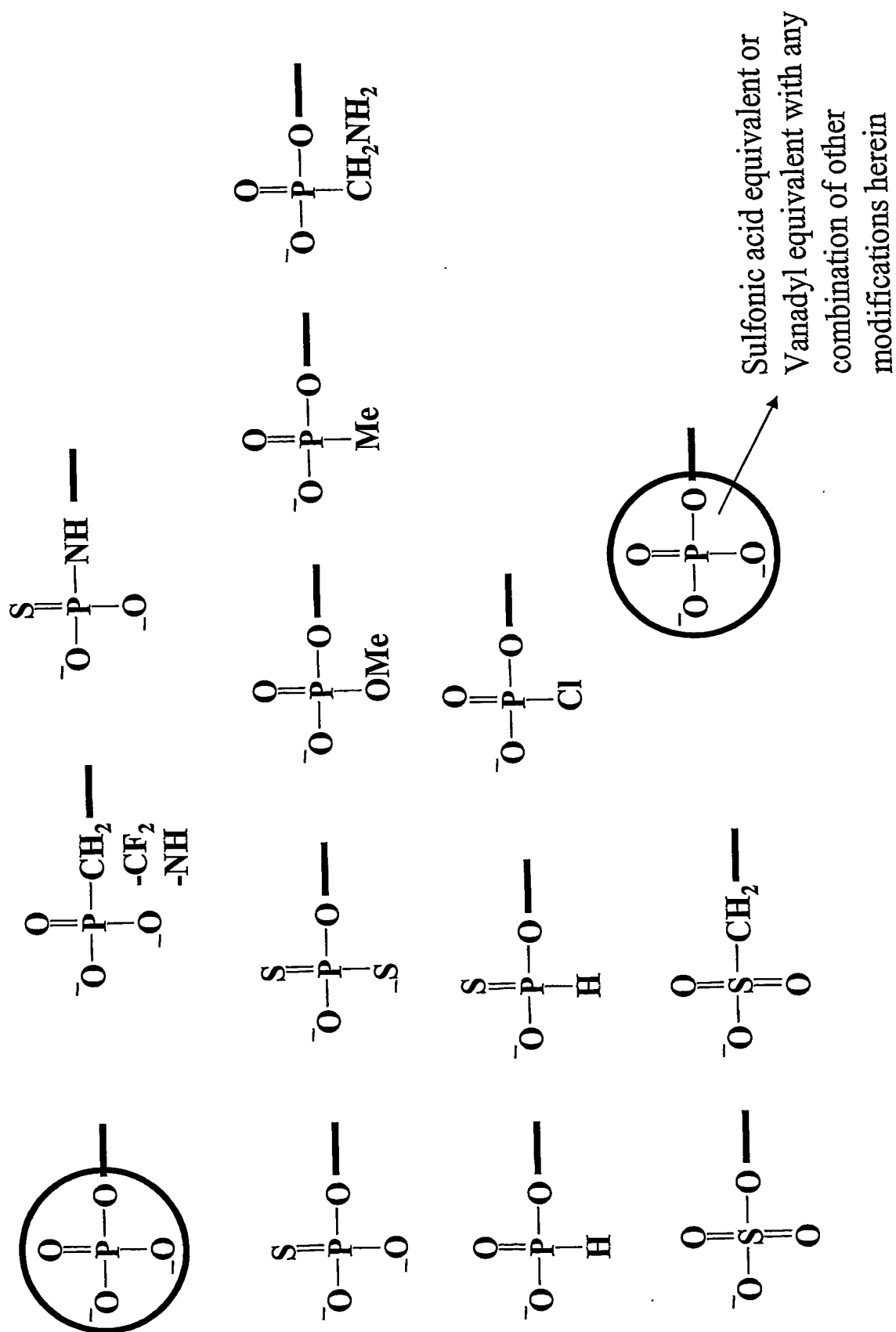


Figure 14A: Duplex forming oligonucleotide constructs that utilize Palindrome or repeat sequences

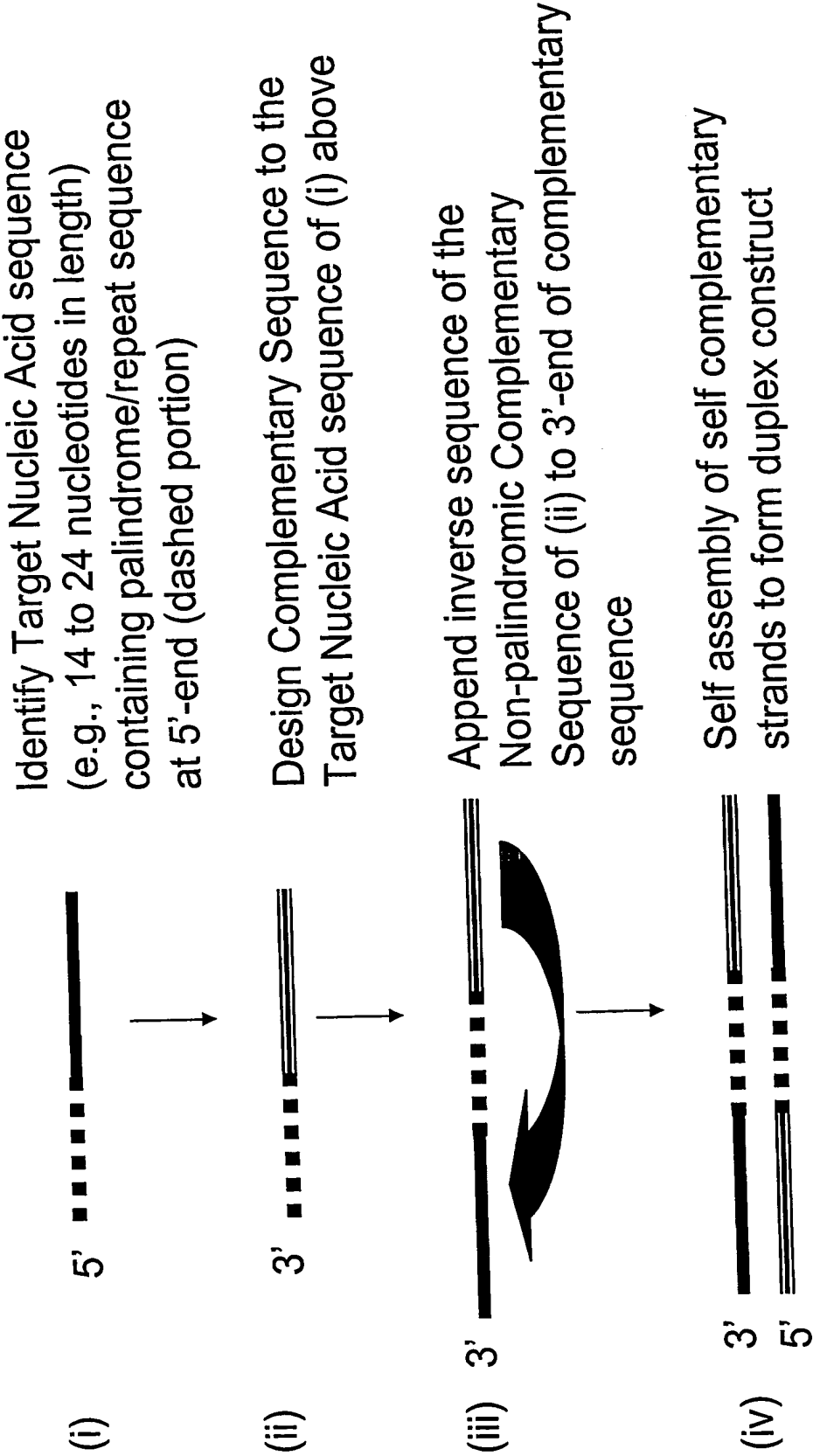


Figure 14B: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence

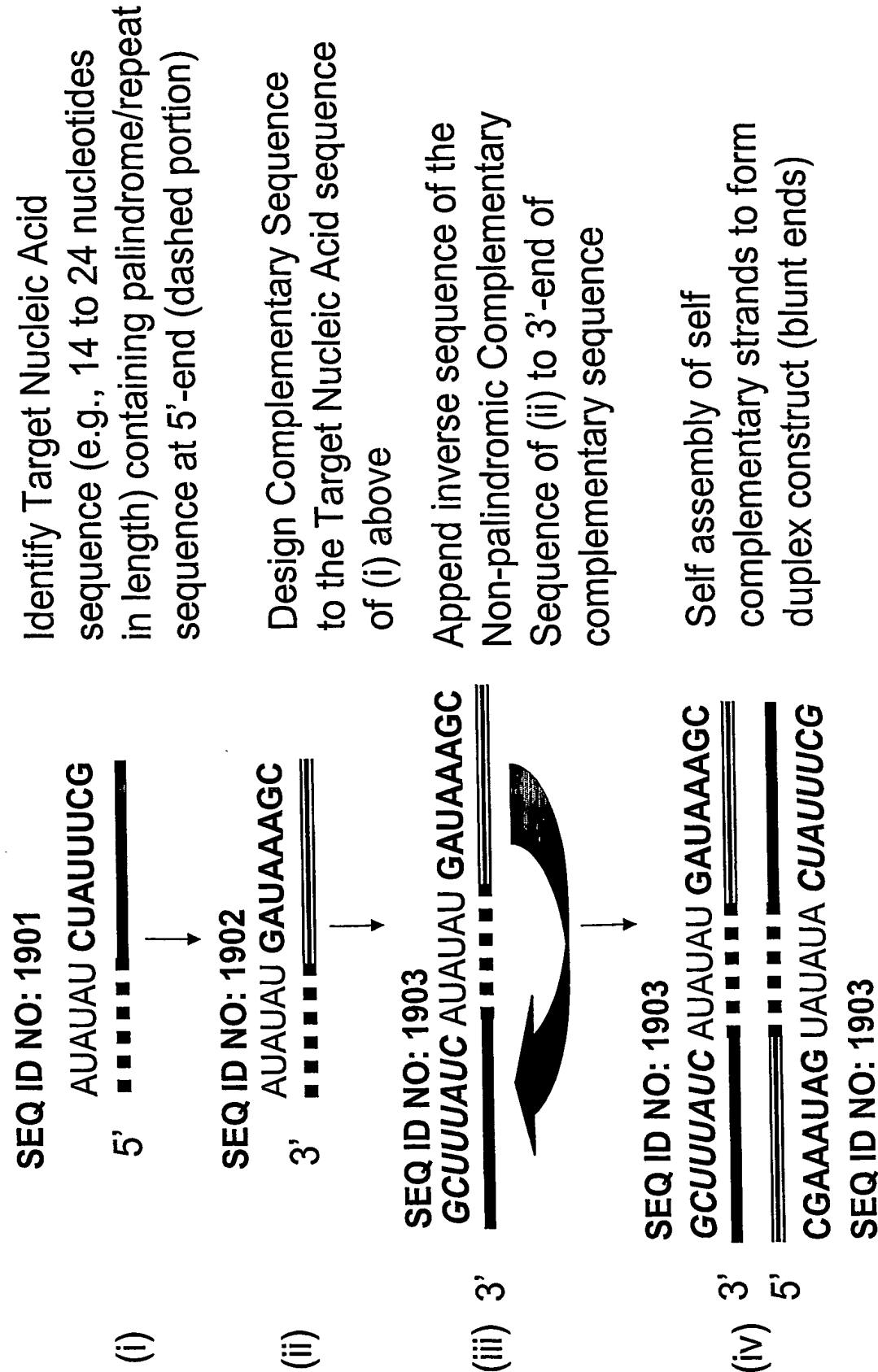


Figure 14C: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly

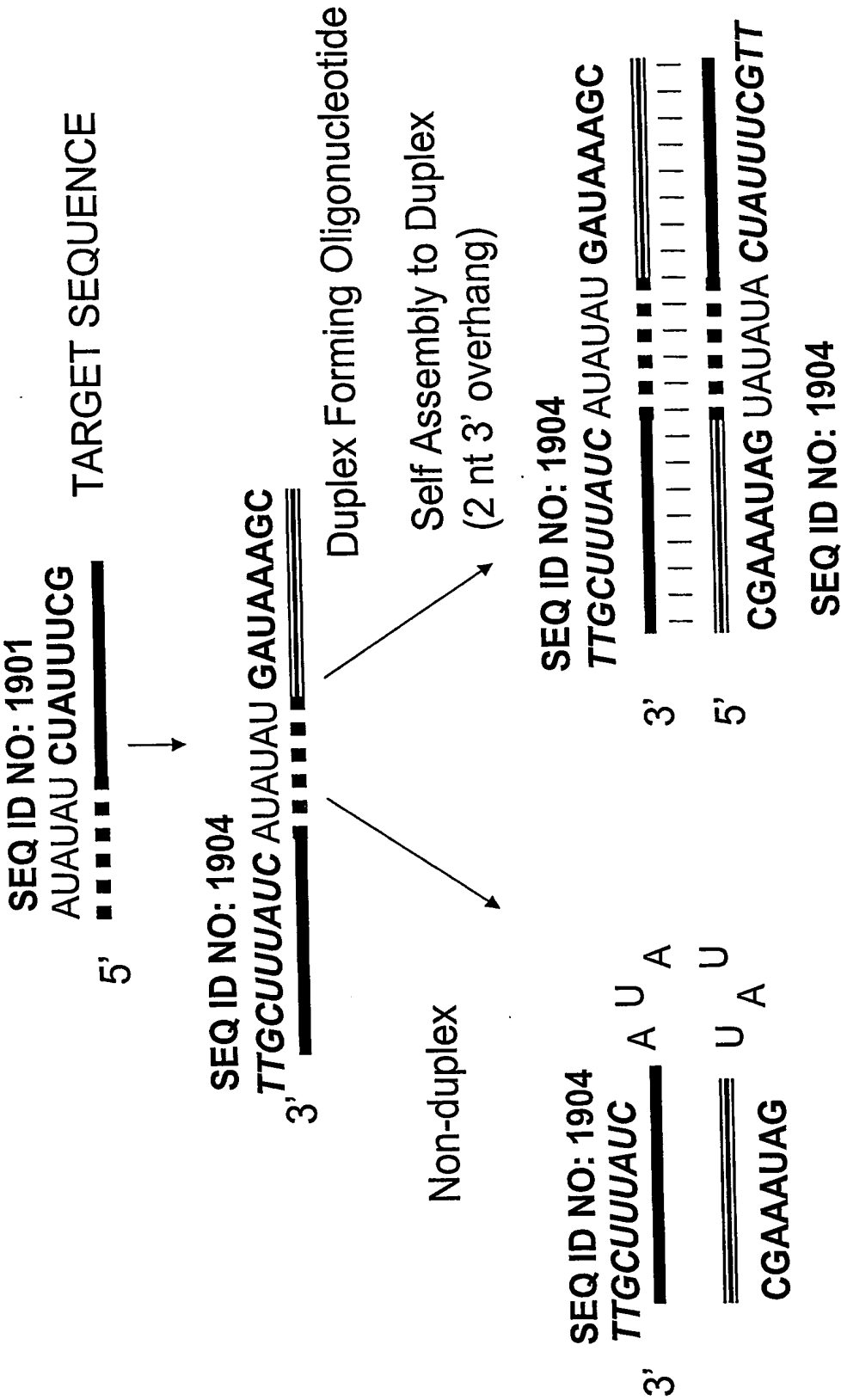
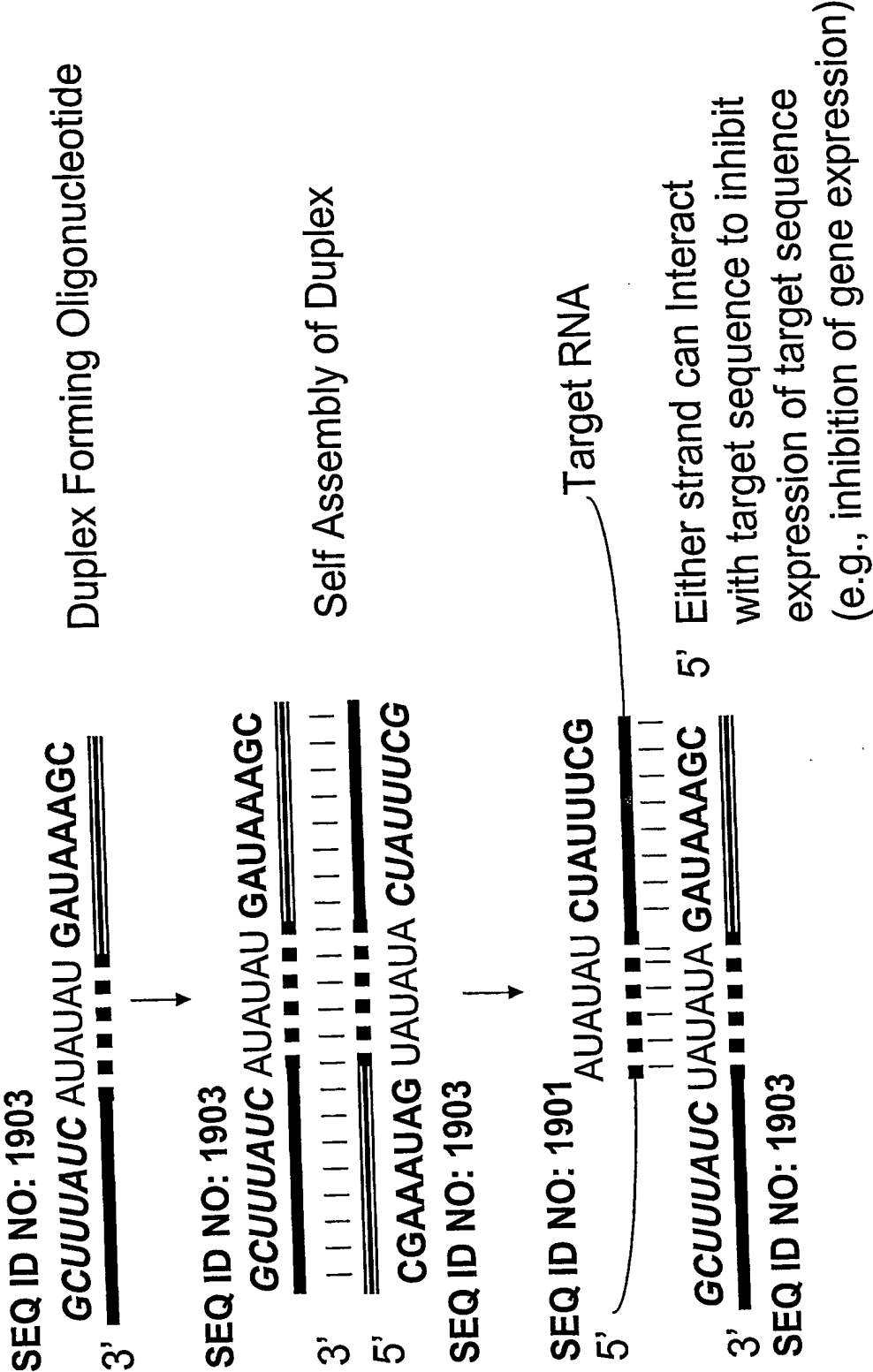


Figure 14D: Example of a duplex forming oligonucleotide sequence that utilizes a palindrome or repeat sequence, self assembly and inhibition of Target Sequence Expression



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Figure 15: Duplex forming oligonucleotide constructs that utilize artificial palindrome or repeat sequences

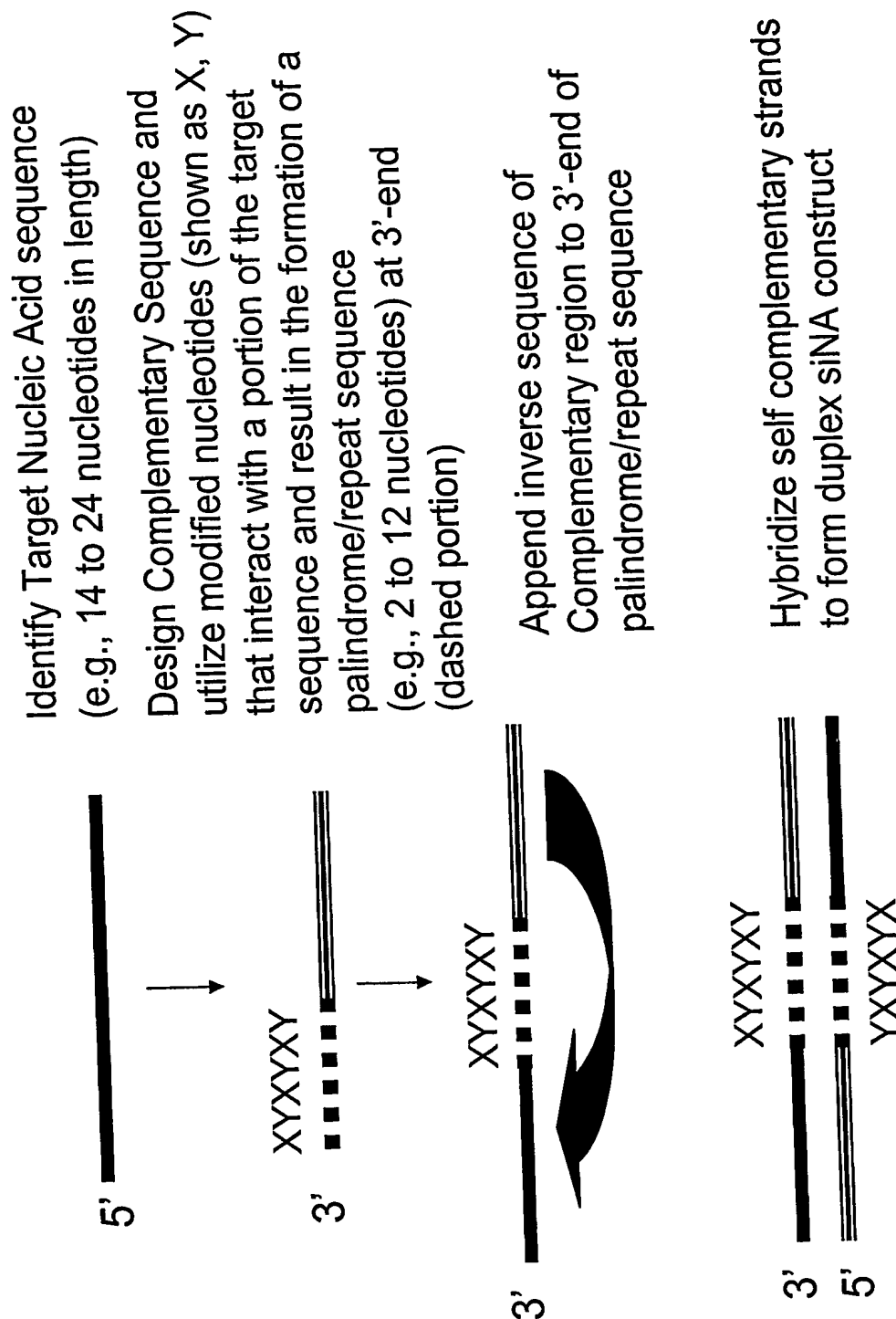


Figure 16: Examples of double stranded multifunctional siNA constructs with distinct complementary regions

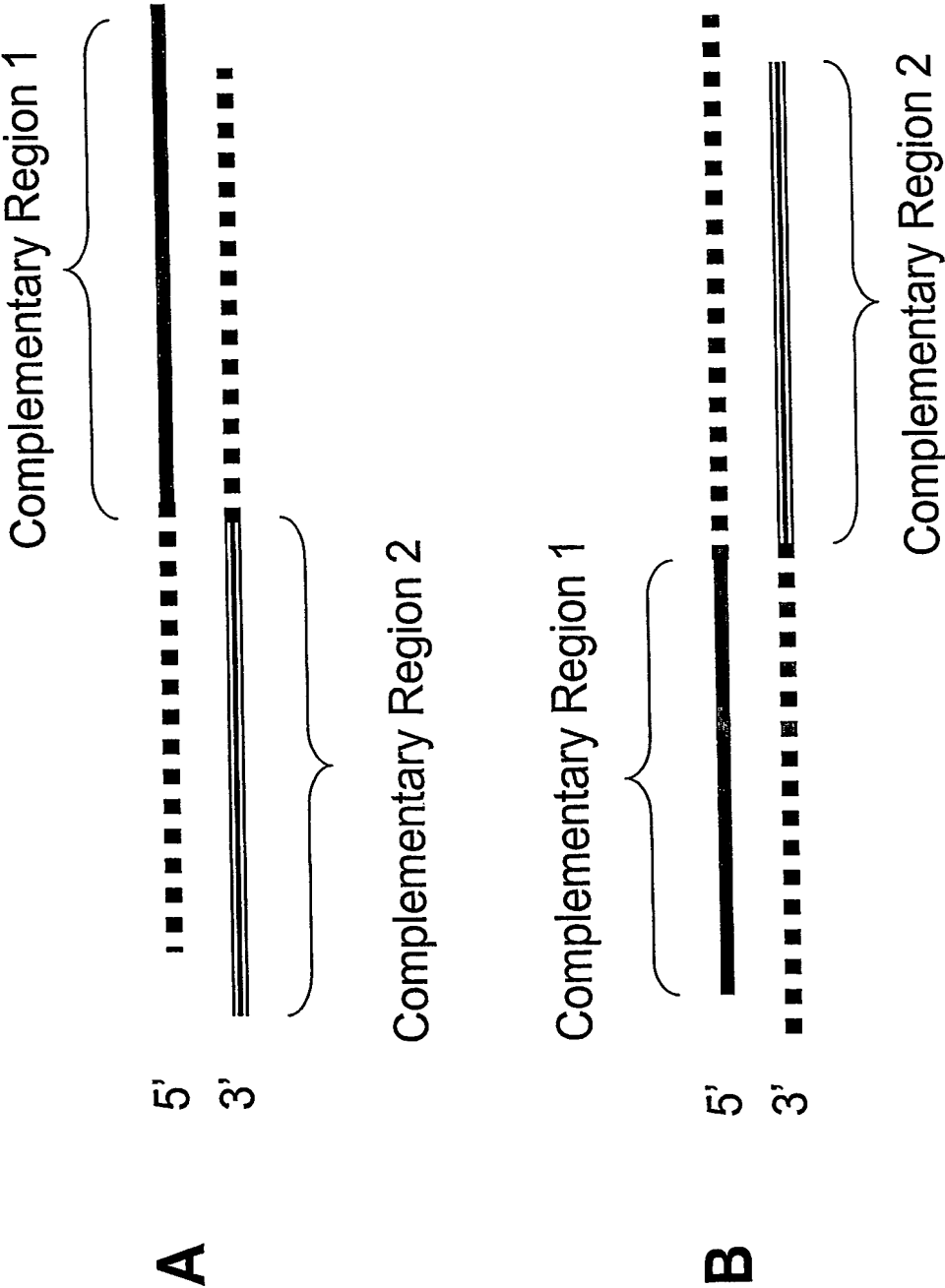


Figure 17: Examples of hairpin multifunctional siNA constructs with distinct complementary regions

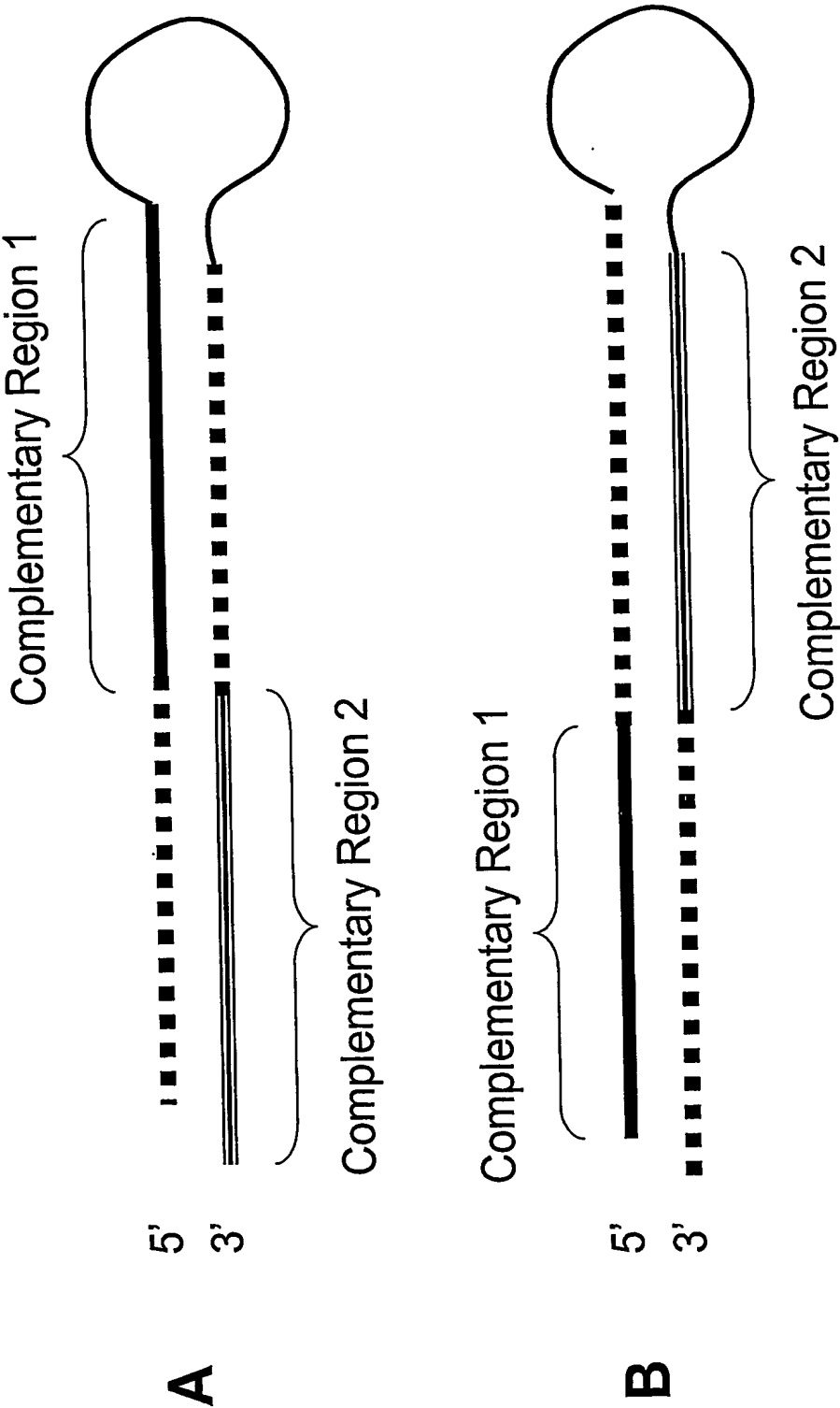


Figure 18: *Examples of double stranded multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region*

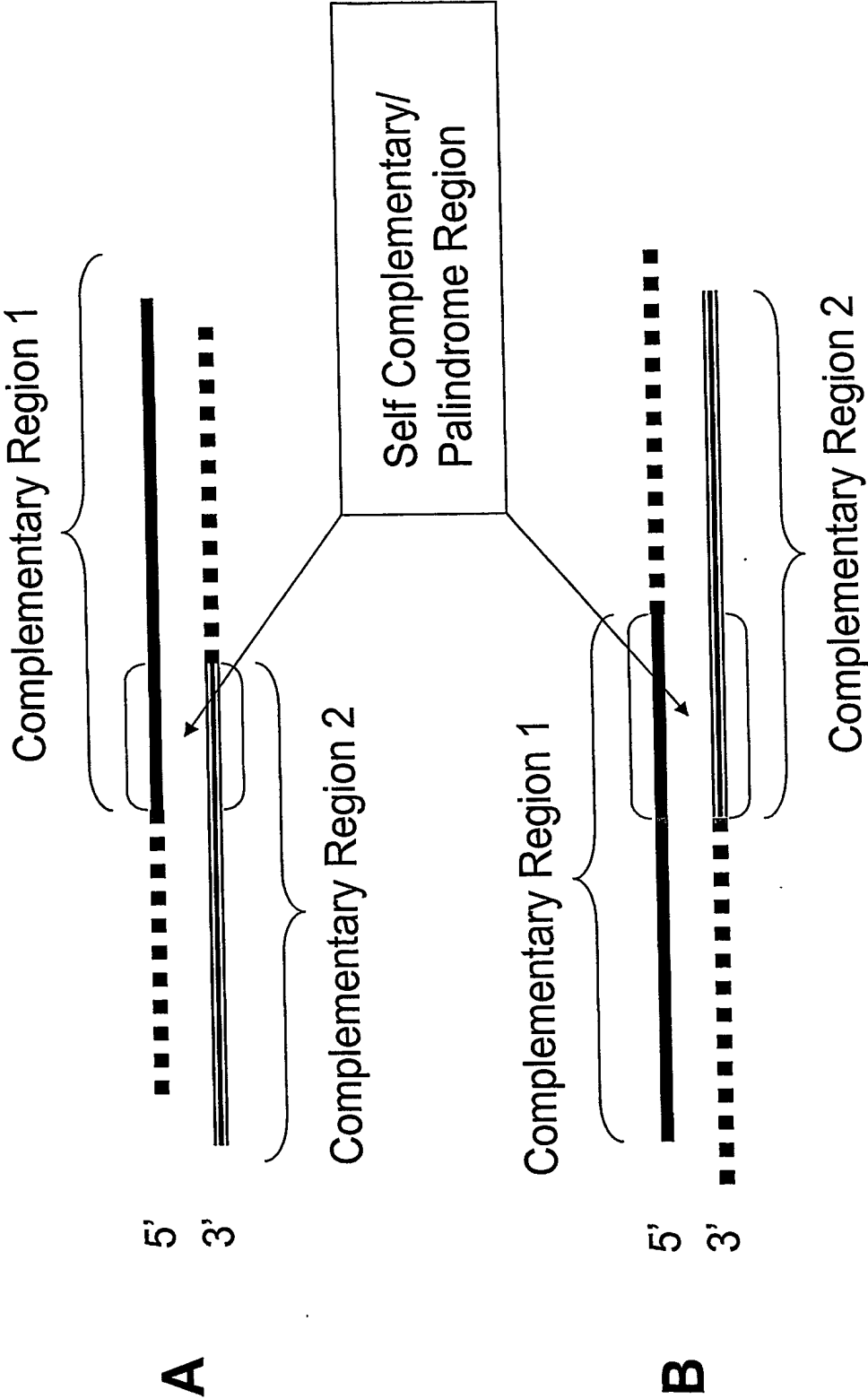
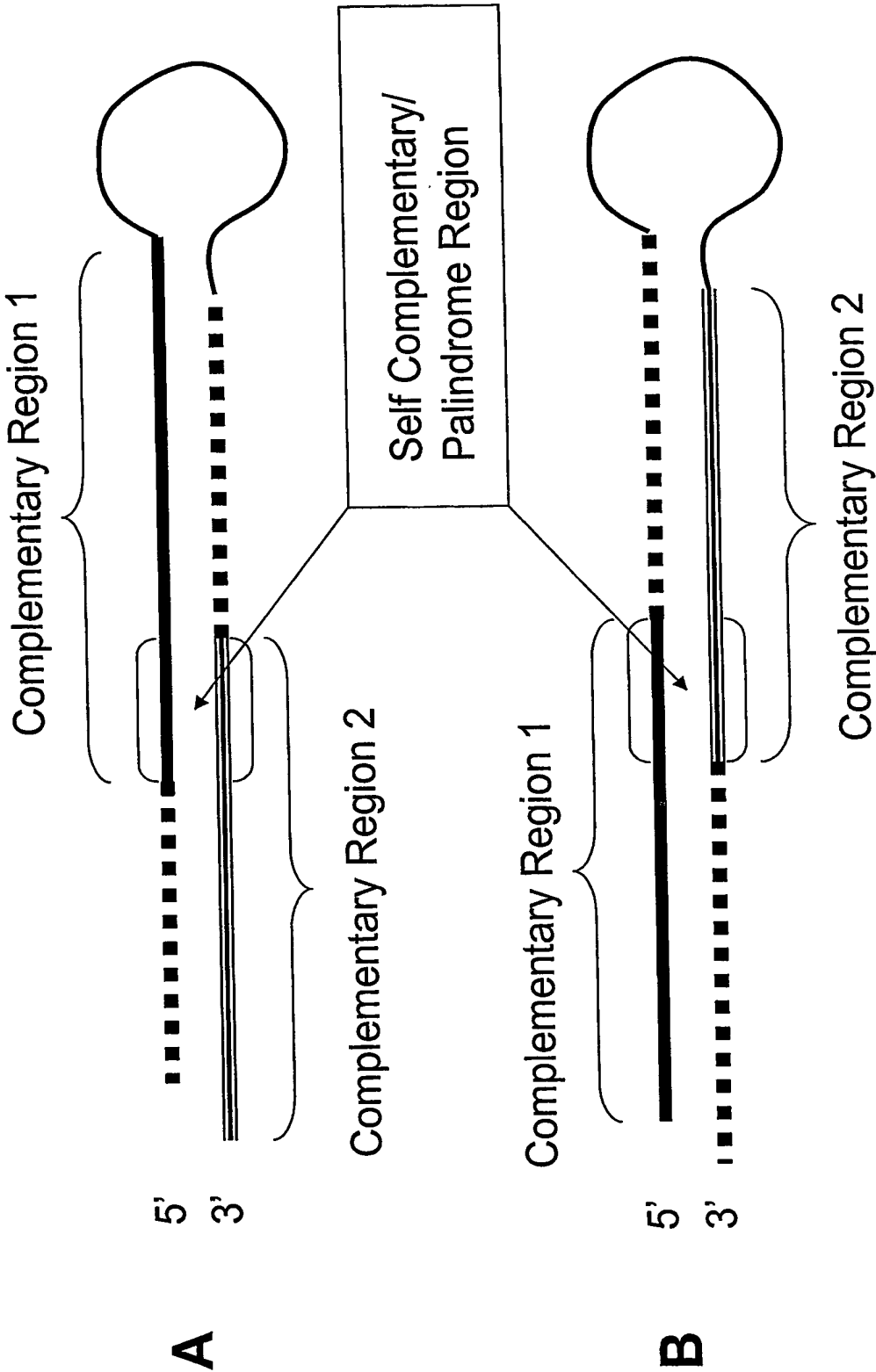


Figure 19: Examples of hairpin multifunctional siNA constructs with distinct complementary regions and a self complementary/palindrome region



**Figure 20: Example of multifunctional siNA targeting two
Separate Target nucleic acid sequences**

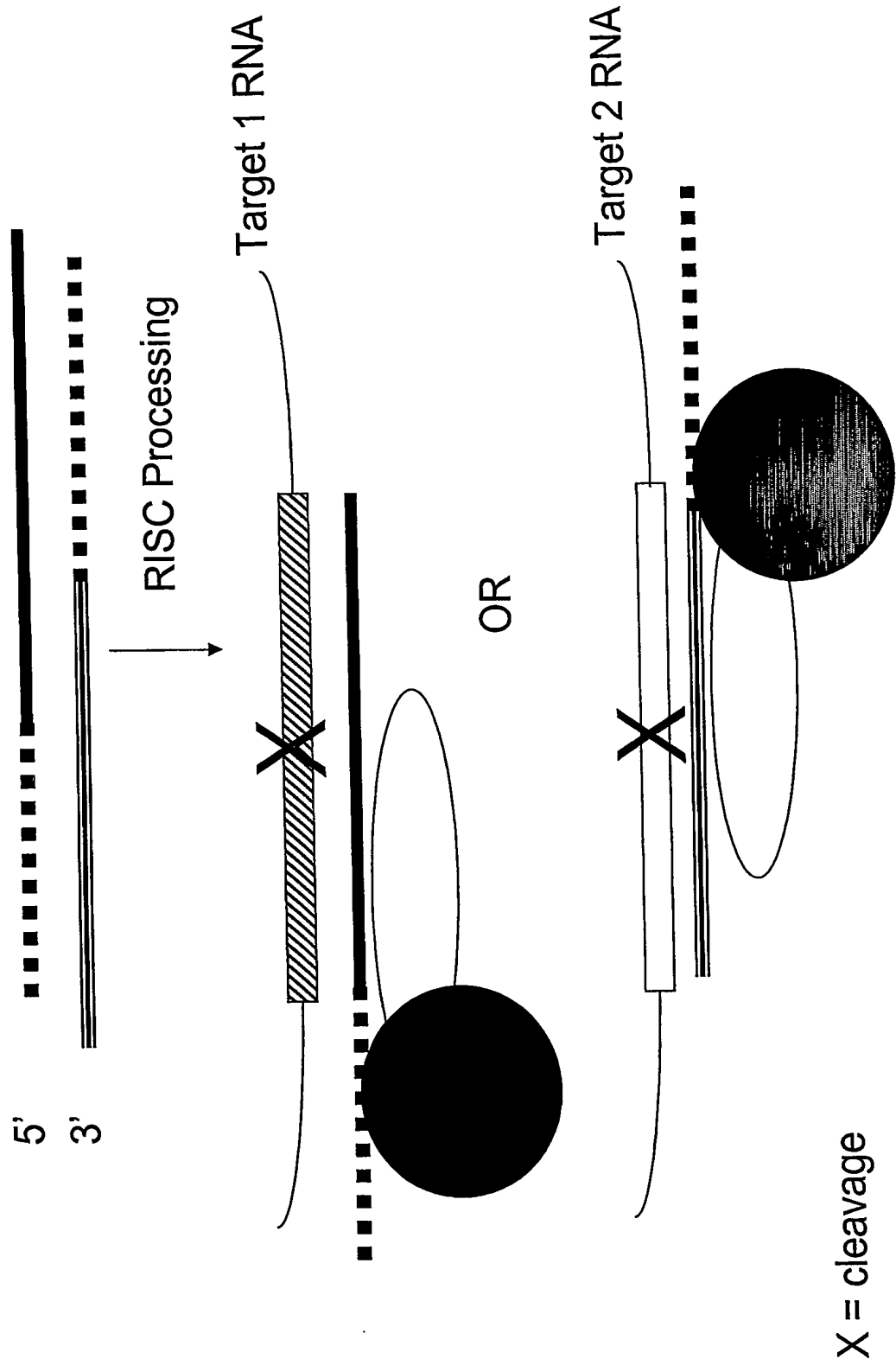
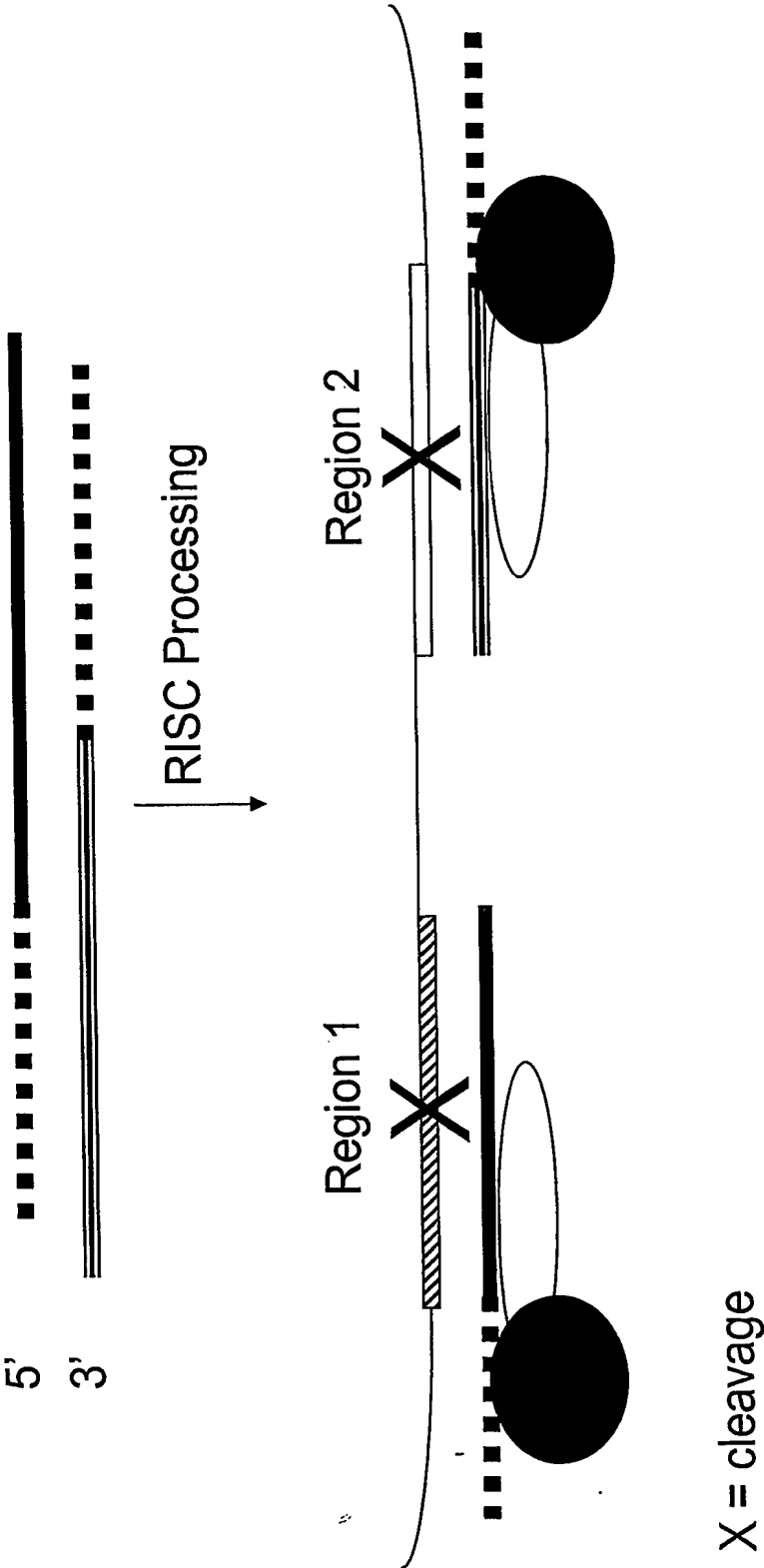
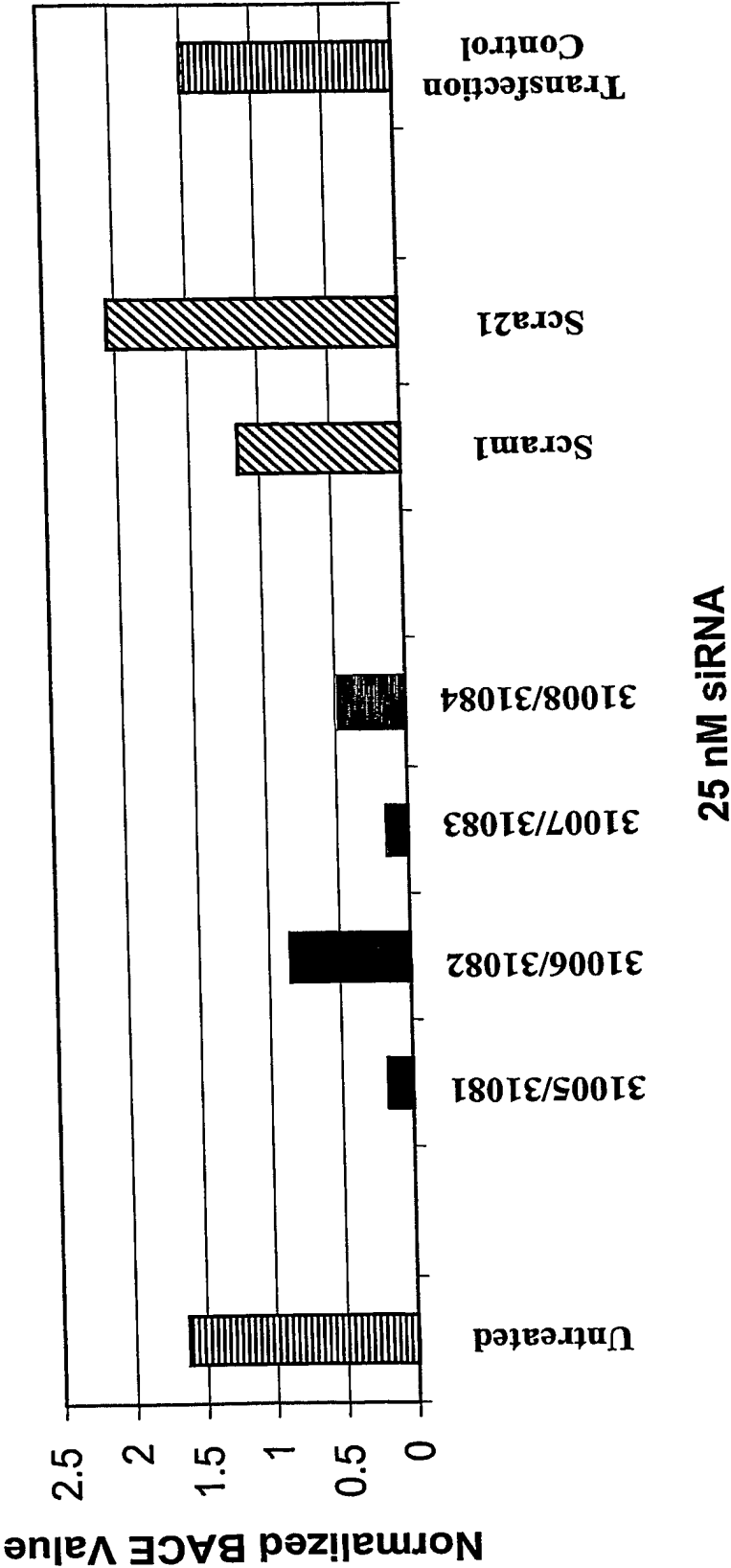


Figure 21: Example of multifunctional siNA targeting two regions within the same target nucleic acid sequence



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Figure 22: A549 24h BACE mRNA Expression



**Figure 23: A549 24h BACE mRNA Expression
using modified siNA**

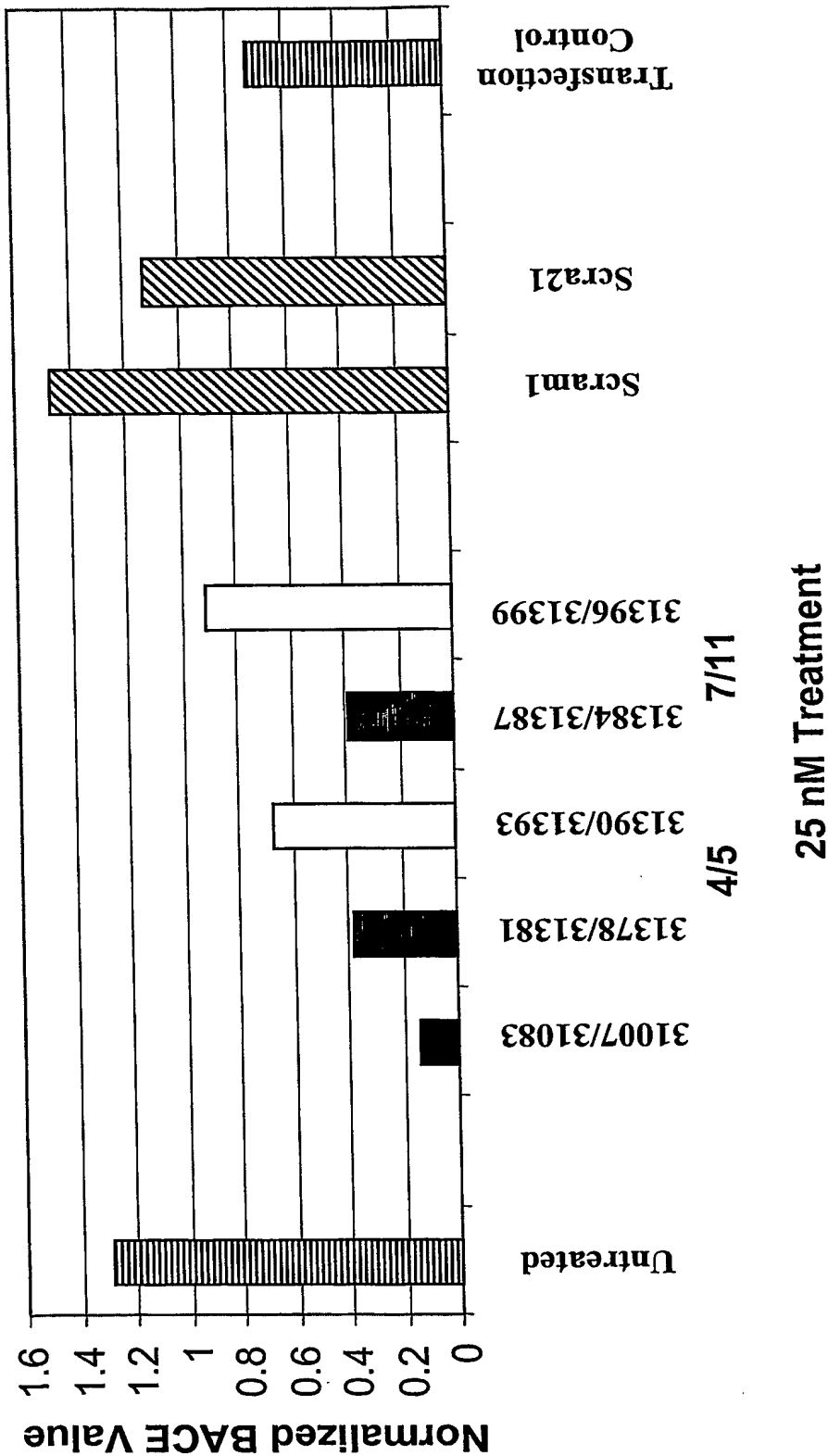


FIGURE 24

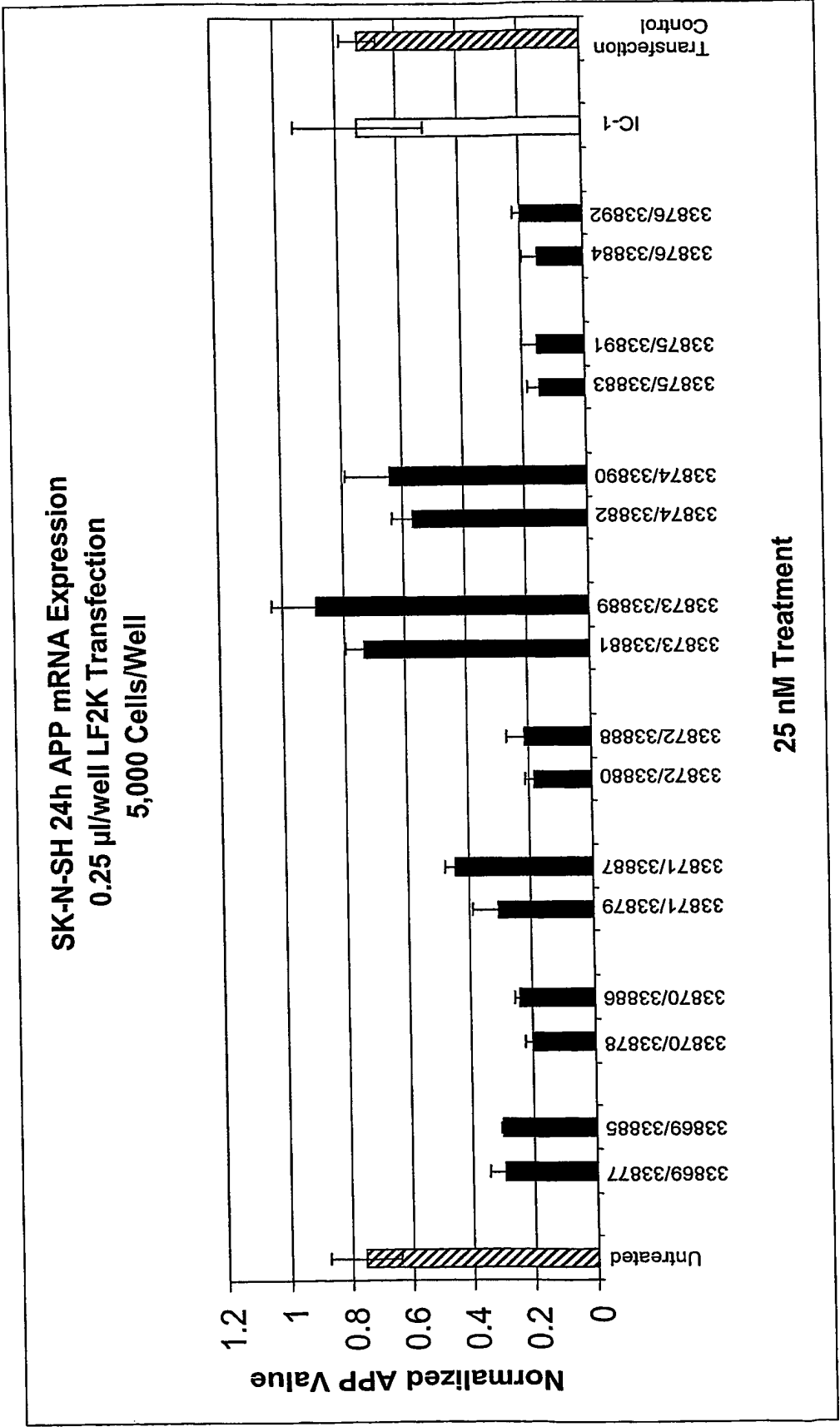


FIGURE 25

SK-N-SH 24h PSEN1 mRNA Expression
0.25 μ l/well LF2K Transfection
5,000 Cells/Well

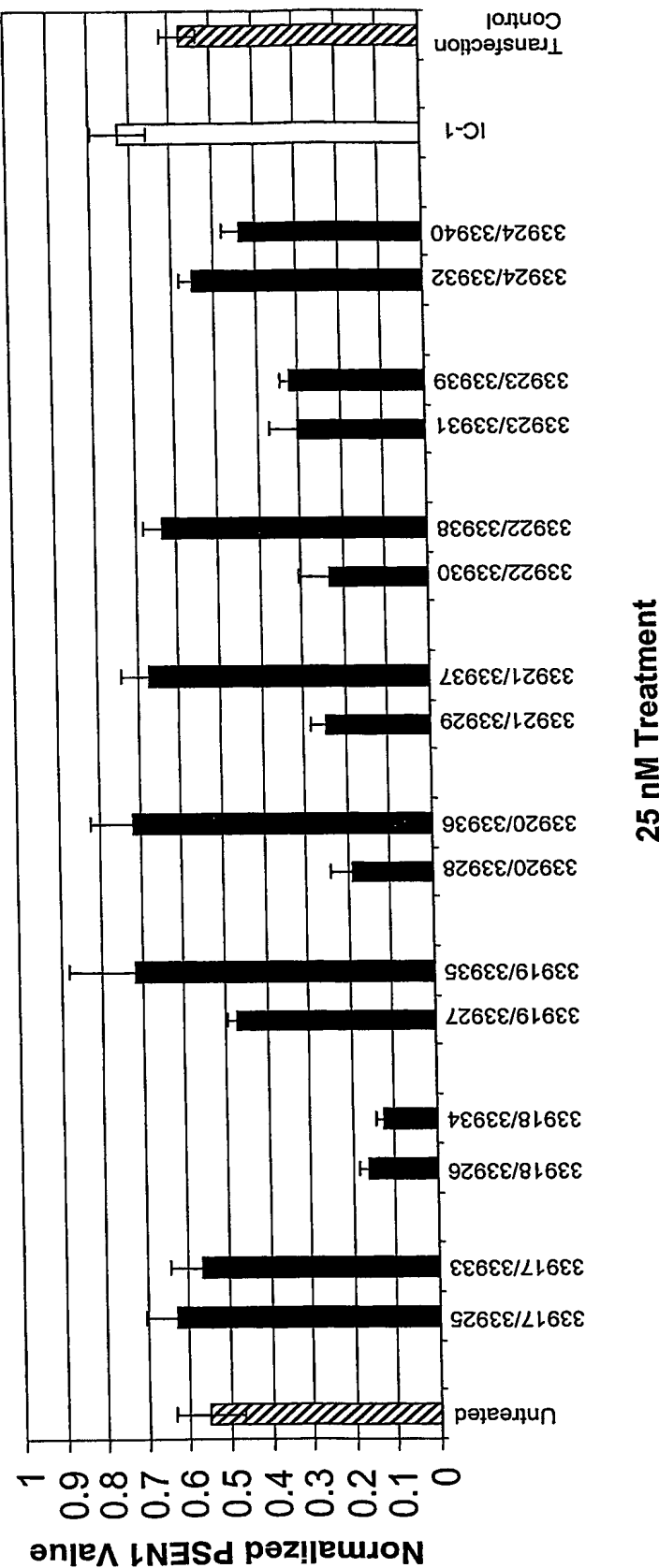


FIGURE 26

SK-N-SH 24h PSEN2 mRNA Expression
0.25 µl/well LF2K Transfection
5,000 Cells/Well

